ORIGINAL ARTICLES

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Chemical Terrorism for the Intensivist

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ABSTRACT   The use of chemical agents for terrorist attacks or military warfare is a major concern at the present time. Chemical agents can cause significant morbidity, are relatively inexpensive, and are easy to store and use. Weaponization of chemical agents is only limited by the physicochemical properties of some agents. Recent incidents involving toxic industrial chemicals and chemical terrorist attacks indicate that critical care services are frequently utilized. For obvious reasons, the critical care literature on chemical terrorism is scarce. This article reviews the clinical aspects of diagnosing and treating victims of chemical terrorism while emphasizing the critical care management. The intensivist needs to be familiar with the chemical agents that could be used in a terrorist attack. The military classification divides agents into lung agents, blood agents, vesicants, and nerve agents. Supportive critical care is the cornerstone of treatment for most casualties, and dramatic recovery can occur in many cases. Specific antidotes are available for some agents, but even without the antidote, aggressive intensive care support can lead to favorable outcome in many cases. Critical care and emergency services can be overwhelmed by a terrorist attack as many exposed but not ill will seek care.

INTRODUCTION

Chemical agents have been used as weapons for centuries with the earliest reports on chemical warfare coming from the Peloponnesian war where burning fumes of coal and sulfur where used by the allies of Sparta.[1] The Byzantine Greeks in 660 CE used noxious fumes containing sulfur, rosia, pitch, naphtha, saltpeter, and lime as toxic chemical weapons ("Greek Fire").[1] The nineteenth century brought significant advance in chemistry crucial to chemical warfare. Despite numerous treaties that banned using them, chemical weapons were first introduced during World War I. German troops used dianisidine chlorosulfonate-laden shells (ineffectively) and, later on, xylyl bromide and chloride. Sadly, chlorine did prove to be effective, and after the German release of 150 tons of chlorine gas from 6000 gas cylinders near Ypres, significant casualties resulted. The French and Algerian troops suffered 800 casualties, and troop movements (on both fronts) were severely hindered; modern chemical warfare had begun.[1,2] During the following decades, several chemical weapons were synthesized. The cyanide-containing insecticide Zyklon B and the nerve agents were developed in Germany. Although the first nerve agent was used in the genocide of thousands of Jews in concentration camps, they were not used as battlefield agents until the Iraq–Iran war. In more recent years, Saddam Hussein used either nerve agents or cyanide against Kurdish citizens in Iraq causing many deaths. In 1994 and in 1995, the Japanese cult Aum Shinrikyo used Sarin in Tokyo causing few casualties, some injuries, and many "worried well."[1–3]

In the event of a chemical terrorist attack, it is likely that critical care physicians would play a key role in managing victims. Chemical agents cause (among others) airway injury, pulmonary edema, bronchospasm, acidosis, coma, seizures, and shock, all of which require intensive care unit (ICU) management. Naturally, the extent of involvement will depend on host, environment, and agent factors, and not all patients will require critical care. Significant injuries are also affected by the length of time of exposure, the distance from the agent, and the concentration of the chemical. In a recent accidental toxic

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Report Documentation Page

1. REPORT DATE **MAY 2012**	2. REPORT TYPE	3. DATES COVERED **00-00-2012 to 00-00-2012**
4. TITLE AND SUBTITLE **Chemical Terrorism for the Intensivist**		5a. CONTRACT NUMBER
		5b. GRANT NUMBER
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)		5d. PROJECT NUMBER
		5e. TASK NUMBER
		5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **415th Chemical Brigade,Greenville,SC,29605 ...**		8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)		10. SPONSOR/MONITOR'S ACRONYM(S)
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES
MILITARY MEDICINE, Vol. 177, No. 5, May 2012

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT **unclassified**	b. ABSTRACT **unclassified**	c. THIS PAGE **unclassified**	**Same as Report (SAR)**	**7**	

industrial release of chlorine in South Carolina, 35% of the patients admitted to the hospital required ICU care.[4] The principles of managing chemical terrorism victims are similar to those of managing toxic industrial chemicals, but this review will focus on treating victims of chemical terrorism.

CLASSIFICATION

There are multiple classification schemes for chemical warfare agents, but for the purpose of this review, we will use the traditional military classification. Agents are classified mainly on the basis of the organ system they affect.[1] Traditionally, chemical warfare agents have been classified into lung agents, blood agents, skin or vesicant agents, and nerve agents. This classification, although simple and time-honored, has several shortcomings. Lung agents can affect other organs, and airway compromise may be more prominent than lung compromise. Blood agents interfere with oxygenation and tend to cause tissue hypoxia and acidosis without affecting clotting or other hematologic functions. Skin agents may have systemic consequences. Nerve agents may have central and peripheral manifestations.[2,5] Table I describes the principal characteristics of the most common chemical agents.

GENERAL PRINCIPLES OF INTENSIVE CARE MANAGEMENT OF CHEMICAL TERRORISM

There are some specific nuances to the management of chemical terrorism victims that the intensivist needs to understand.[6] Chemical terrorism patients may have more than one affliction, and it is easy to overlook other medical problems because of the dramatic presentation of chemical attacks. Trauma may coexist with chemical poisoning, and an open wound can serve as an additional source of entry. Biological and chemical terrorism may coexist, and since biological agents tend to have delayed presentation, this could potentially lead to misdiagnosis. During a given attack, victims may present with very different syndromes because of host factors, route of exposure, speed of decontamination, and exposure dose. Patients may seem stable early on and later decompensate (lung agents). Patients with severe organ dysfunction may recover completely even though the initial clinical examination suggests that the situation is hopeless.[3] Lessons from prior chemical incidents suggest that prehospital airway management can be complicated by limited resources and increased technical demands; therefore, the intensivist needs to be prepared to provide an airway and to deal with the consequences of delayed intubation.[6] Chemical agents may interact with medicines used in the ICU, and the clinician needs to be mindful of this interaction (nerve agents and neuromuscular blockers).[6] Chemical and biological attacks are resource-intense events that can easily overwhelm the health system, and a planned emergency response needs to be in place a priori.

LUNG AGENTS

Lung agents (exemplified by chlorine and phosgene) are one of the most likely chemical weapons to require critical care. Chemical agents can affect airway, breathing, pulmonary gas exchange, and oxygen transport.[5,7] The specific clinical manifestations will depend on the agent, time of exposure, concentration, speed of removal and decontamination, and host factors.[2] It is useful to categorize patients into those suffering central injury (oropharynx, larynx, vocal cords, trachea), peripheral injury (alveoli), or mixed injury. Patients with central injury may require early intubation and mechanical ventilation because of imminent obstruction. Patients with peripheral injury may appear compensated early on but after a latency period (usually 24 hours) will develop hypoxemia. Moderate to severe exposures may result in marked pulmonary edema in less than 4 hours because of damage to

TABLE I. Characteristics of Common Chemical Terrorism Agents

	Lung Agents	Blood Agents	Vesicants	Nerve Agents
Classic Examples	Chlorine, Ammonia, Phosgene	Cyanide, Carbon Monoxide	Sulfur Mustard, Lewisite	Tabun (GA), Sarin (GB), Soman (GD), VX
Route of Exposure	Inhalation	Inhalation, Ingestion	Skin Exposure, Corneal Exposure, Inhalation, Ingestion	Skin Contact, Wound Penetration
Clinical Symptoms	Nose, Throat, Eye Irritation, Cough, Stridor, Wheezing, Frothy Sputum	Headache, Fatigue, Anxiety, Irritability, Cardiac Arrest, Dyspnea Coma, Seizures	Conjunctivitis, Sore Throat, Epistaxis, Erythema, Skin Blisters, Corneal Ulceration, Wheezing, Stridor, Acute Lung Injury, Immunosuppression	Miosis, Dim Vision, Increased Secretions, Wheezing, Fasciculations, Flaccidity, Coma, Seizures
Paraclinical Findings	Abnormal PaO_2/FIO_2, Acute Lung Injury or ARDS Pattern on Chest X-ray, Cardiomegaly	Lactic Acidosis, Anion Gap, High Cyanide Level, Electrocardiogram Changes	Leucocytosis Followed by Leucopenia, Elevated Sedimentation Rate, High Thiodiglycol Levels, Alveolar Infiltrates	Decreased Cholinesterase Levels, Lactic Acidosis, Elevated CK, Depressed Adrenal Function (Sarin)
Treatment	Supportive	Sodium Nitrite, Thiosulphate	Supportive, British Anti-Lewisite (Lewisite)	Atropine, Oximes, Benzodiacepines

the alveolar-capillary membrane barrier. In general, highly soluble agents (ammonia) will preferentially affect central airways, whereas less soluble agents (phosgene) will affect peripheral airways.[2] Agents that are usually nonlethal such as riot control agents may be lethal in individuals with underlying lung disease.[2]

The biochemical and cellular events that follow exposure to phosgene are well understood.[8] Phosgene reacts with sulfhydryls, amines, and hydroxyl groups. Additionally, phosgene can deplete type I pneumocytes, increase lavage polymorphonuclear phagocytes, decrease cytochrome c-oxidase, decrease ATPase activity, and deplete lung ATP levels.[9] Many of the clinical findings seen in phosgene intoxication are related to increased leukotriene production and decreased c-AMP levels. The clinical implication of such findings is that treatment efforts should be aimed at upregulating cAMP levels and antagonizing leukotrienes.[8,10]

The clinical presentation of patients exposed to respiratory agents is fairly characteristic, but the time from exposure to symptom development varies depending on host and environmental factors. Highly soluble agents will cause early symptoms, whereas poorly soluble agents will cause delayed symptoms.[2,5] Central agents will cause immediate nasopharyngeal pain, coughing, sneezing, laryngospasm, and wheezing. On clinical examination, erythema, swelling, and desquamation of the upper airways may be evident. Hoarseness and stridor on expiration raise concern for possible airway obstruction.[2] Peripherally acting agents will initially cause subtle symptoms such as irritation of the eyes, nose, and throat. Within 24 to 72 hours, most casualties will notice progressive dyspnea, increasing cough, and production of clear, foamy sputum. Dyspnea is usually increased by exercise, and strict bed rest is recommended. In a recent case of toxic exposure to chlorine, the most common clinical findings were tachypnea, tachycardia, wheezing, and rales. Hypoxia on room air predicted development of acute lung injury and acute respiratory distress syndrome.[4]

Adjunct diagnostic study findings in patients exposed to lung agents are related to the severity of the exposure. Patients requiring ICU care will almost invariably have abnormal arterial blood gases and abnormal chest X-rays. In the Graniteville chlorine spill, 22% of patients had arterial blood gas findings suggestive of acute lung injury and 53% had findings suggestive of acute respiratory distress syndrome.[4] Imaging findings usually appear after 24 hours and include parenchymal densities, alveolar infiltrates, atelectasis, noncardiogenic pulmonary edema, and bilateral consolidation.[4,11] The initial chest X-ray in phosgene victims may be normal, but follow-up X-rays performed 6 to 12 hours later may show an acute respiratory distress syndrome pattern. Pulmonary function tests reveal a restrictive or obstructive pattern. In patients exposed to phosgene, hypotension, volume depletion, and noncardiogenic pulmonary edema are common.[2,7] Cardiomegaly appears to be a frequent finding among fatalities exposed to chlorine, but the implication of such finding is unclear.[4]

Management of patients exposed to lung-damaging agents is largely supportive. Patients should be intubated early on if there is evidence of central airway compromise with impending obstruction. Increased secretions and vomiting are frequent, and intubation facilitates suctioning and helps prevent aspiration.[5,12] Central-acting agents (ammonia) can lead to unexpected airway obstruction and early intubation is warranted in moderate to severe cases. Mechanical ventilation should be instituted using a lung-protective strategy as there is a high incidence of acute lung injury and acute respiratory distress syndrome. Prophylactic antibiotics are not needed, but close monitoring for development of pneumonia is imperative. When pneumonia does occur, it usually occurs between days 3 and 5. Steroids and beta-agonists are commonly used, and although there is no strong human clinical data to support this practice, there is some animal evidence that supports it.[8,9] Observational studies suggest that inhaled $NaHCO_3$ may ameliorate chlorine-induced lung injury.[13] In animal studies, furosemide was not of any benefit in treating phosgene-induced acute lung injury.[10] Furthermore, phosgene victims are often volume depleted (because of capillary leak) and require volume replenishment.[7] Most fatalities occur in the first few hours and surviving victims usually recover with meticulous supportive ICU care.[2]

BLOOD AGENTS

Blood agents or asphyxiants (exemplified by hydrogen cyanide and cyanogen chloride) are agents that cause toxicity by interfering with cellular oxygen use. Cyanide is considered one of the most likely agents to be used in a terrorist chemical attack.[14] Cyanide is widely available, inexpensive, requires little knowledge to be used, and is very lethal. Weaponization of cyanide is limited by the fact that it is a very volatile agent, and although battlefield use is difficult, use as a terrorist weapon in a confined space is possible.[14,15] In addition, warfighters can be exposed to cyanide as a result of combustion of wide variety of synthetic materials.[2] Two American soldiers required prolonged ICU management after being exposed to cyanide and heroin that were deliberately added to smokeless tobacco during Operation Enduring Freedom (Stars and Stripes report 6, September 2008). The cyanide anion preferentially forms a complex with the ferric iron (Fe^{3+}) in the cytochrome oxidase system interfering with cellular respiration. The ensuing depletion of ATP results in anaerobic metabolism and acidosis.[11] The usual mechanism of death is central apnea.

As in most toxic exposures, the degree of exposure and the underlying vulnerability of the host will determine the clinical presentation. In most cases, the initial symptoms of cyanide exposure are nonspecific, but may include a cold sensation in the nose and upper airway as well as the smell of bitter almonds. Unfortunately, only 50% of the European population has the gene needed to be able to detect the bitter almond smell.[11] Neurologic symptoms follow the premonitory symptoms with headache, dizziness, and vertigo being

most common. Afterwards, central apnea (sometimes preceded by hyperpnea), coma, opisthotonic posturing, and seizures develop. In severe cases cardiac, arrest will ensue in approximately 5 minutes.[15] Intensivists will most likely encounter mild to moderate cases who survived to reach ICU care or fortunate victims who received prompt first aid and antidote.[1,2,16] Severe cases are defined as those with unconsciousness. Cyanide is present in many furniture products and burns immediately when ignited. In a large series of cyanide intoxication after fires, cardiac disturbances were found to be common.[15] Cardiac arrest (usually asystolic) occurred in 40% of victims reaching the hospital. Cardiac arrhythmias (mainly supraventricular tachycardias), conduction disorders, and repolarization abnormalities were common. The survival rate for patients initially seen in cardiac arrest was around 3%.[15]

The clinical examination in cyanide victims deserves special discussion because the findings are often misunderstood. The typical victim is described as pink, flushed, warm, and having an anion gap acidosis without hypoxemia or shock. The fundal vessels may appear bright red.[7] Upon drawing blood, it may be noticed that venous blood has a bright red appearance. Of note, the cherry-red complexion may be as a result of elevated circulating carboxyhemoglobin levels or to highly oxygenated venous blood.[2] Clinicians must be careful not to rely on such signs as cyanide poisoning victims may be cyanotic or have a normal complexion.[2] Severe respiratory distress in the absence of cyanosis is however a useful clinical sign. The very rapid evolution of the signs and symptoms is a useful diagnostic clue.[6]

Adjunct studies are essential in confirming cyanide poisoning. The most characteristic laboratory finding is a metabolic acidosis with elevated anion gap.[2,5] An elevated cyanide level (above 2.5 mcg/mL) is associated with coma, and lower levels are seen in patients with mild to moderate symptoms. Lactic acid levels may be elevated, and venous oxygen concentration will show an unusually high oxygen level. The electrocardiography may show supraventricular arrhythmias, conduction abnormalities, and repolarization changes.

Cyanide poisoning victims require intubation if they have decreased level of consciousness, frequent seizures, apnea, hypoxemic or hypercapnic respiratory failure, or profound acidosis.[12] In addition, patients with coexisting burns in the upper airway should receive early intubation. Nonintubated patients should receive 100% O_2 via nonrebreather mask as this will help eliminate carbon dioxide.[2] Patients in shock (usually cardiogenic) should be treated with inotropes and with judicious administration of fluids. Patients with seizures should receive intravenous lorazepam as needed for seizure control. Activated charcoal should be used if the agent was ingested and the gastric contents discarded carefully because of risk of contamination. Intravenous bicarbonate can be administered as a temporizing measure, but the definitive treatment is antidote administration. In the United States, cyanide poisoning is treated by administering the Lilly Antidote Kit, which contains sodium nitrite and thiosulfate.[5] Nitrite forms methemoglobin, which has a very high affinity for cyanide, and this compound is then metabolized by the liver enzyme rhodanase (with the help of thiosulfate). Clinicians need to be wary of the fact that methemoglobinemia may worsen the oxygen capacity of the blood in patients with coexistent elevated carboxyhemoglobin levels.[2,5] Nitrite administration may cause hypotension that can worsen already compromised cardiac and neurologic function. Some experts suggest using oxygen and thiosulfate without nitrites in smoke-inhalation victims because of possible elevated carboxyhemoglobin levels.[2] In other countries, hydroxocobalamin is the preferred antidote.[14]

Patients with cyanide poisoning can recover even when the clinical examination is dismal, and clinicians should aggressively try to support them and administer the antidote if no contraindications exist. Lack of availability of the antidote should not lead to classifying the casualty as expectant, as patients can recover without the antidote provided aggressive critical care support is provided.[2] The usefulness of hyperbaric oxygen in pure cyanide poisoning remains in question.[11]

SKIN OR VESICANT AGENTS

The term "blister" agent is a euphemism for the vesicant agents (exemplified by sulfur mustard and lewisite) as vesicants do have significant systemic toxicity (only 10% of absorbed sulfur mustard stays in the skin).[2] Sulfur mustard (NATO name HD) is a strong alkylating agent with its most prominent effect being the alkylation of DNA.[5] At room temperature, HD is a liquid that easily vaporizes. Rapidly proliferating tissues (eyes, bone marrow, gut epithelium) tend to be affected the most. There is some recent ICU experience with sulfur mustard as it was used by Iraq during the Iraq–Iran war.[17] It is suspected that the Burmese military used vesicants against the Karenni people in 2005.[2] Furthermore, over 70% of all battlefield chemical casualties have been a direct result of HD exposure. A major concern in the event of a terrorist attack with HD is the asymptomatic interval that may follow exposure as it could result in delayed recognition of vesicant toxicity. In all recently described cases of Iranian soldiers exposed to HD, symptoms were delayed for several hours.[17]

The earliest symptoms of HD toxicity are eye pain and irritation occurring within 2 hours of exposure. Shortly after, throat, gastrointestinal, and respiratory symptoms ensue. Skin erythema occurs in 10% of patients within 2 hours of exposure, but vesicles do not appear until at least 4 hours later.[17] Initially, the eyelids become edematous, and the conjunctivae appear red and swollen. Severe blepharospasm is frequent as well as infectious conjunctivitis, corneal opacities, and corneal erosions. Skin lesions are the predominant finding progressing from flat erythematous lesions to large fluid-filled vesicles that are more prominent in intertriginous areas or moist areas. Unexposed moist areas are particularly vulnerable to HD.[17] The vesicles are thin-walled, filled with a clear yellow fluid, and do not contain HD. Skin hypo- or

hyperpigmentation is common as well as keloid scar formation.[2,17] There is no correlation between body surface compromise and mortality from HD.[2] The primary effect of HD is airway irritation initially manifested by rhinorrhea, cough, sneezing, and dysphonia. With increasing doses, tracheobronchitis and pseudomembranous formation occur. Mechanical obstruction from pseudomembranous formation or laryngospasm may be fatal. Superimposed pneumonia can also occur. The gastrointestinal epithelium is very susceptible to the effects of HD, but the clinical manifestations are usually minor. Nausea, vomiting, and diarrhea may occur because of the mild cholinergic effect of HD and radiomimetic gut effects.[2] Neurologic effects of HD are poorly defined, but patients often appear to be somnolent, apathetic, and depressed. There is a potential for seizures as HD is a proconvulsant agent. Myelosuppression is one of the most serious consequences of HD exposure, and patients are at risk of developing superimposed infections.[2,17]

The laboratory findings vary depending on the severity of exposure. In severe cases, an initial leukocytosis will be followed 3 or 5 days later by a rather precipitous leukopenia. A leukocyte count below 500 has ominous prognosis.[17] Other blood cell lines may also be affected. The erythrocyte sedimentation rate becomes elevated as the disease progresses. The initial chest X-ray is usually normal, but alveolar infiltrates appear when superimposed pneumonia develops. The intensivist needs to be mindful that HD patients may develop significant infections without classic laboratory or clinical signs. If the diagnosis is not clear on clinical grounds, measuring thiodiglycol (urinary metabolite of HD) can provide indirect evidence of HD exposure.[2]

The treatment of patients exposed to HD is largely supportive. Airway compromise manifested by dysphonia, stridor, and dyspnea should prompt intubation and mechanical ventilation. Patients with hypoxemic or hypercapnic respiratory failure also require intubation. Pseudomembranous formation causing upper airway obstruction will often require tracheostomy. Cough suppressants, humidified oxygen, mucolytics, and bronchodilators should be used to treat respiratory complications.[2,12,17] Pulmonary infections usually happen after the third day of onset and should be treated with wide-spectrum antibiotics until the specific etiology is determined. The intensivist must keep in mind that the patient may be immunocompromised and at risk for opportunistic infections. The skin lesions are quite painful, and liberal use of opiates is often warranted. Small blisters should be left intact while larger ones should be denuded, cleaned 3 to 4 times a day with saline, and covered with a topical antibiotic such as silver sulfadiazine.[2] Burns from HD can often take twice as long to heal as normal burns, so persistent wound management is imperative. Patients do not develop the fluid loss seen in patients with thermal burns; therefore, crystalloids should be administered judiciously to ensure normovolemia.[2] Eye care should be coordinated with an attending ophthalmologist. Initially, the eyes are irrigated with saline and anticholinergic eye drops and topical antibiotics are prescribed.

Vaseline should be applied to the eyelids to prevent them from adhering. Granulocyte colony-stimulating factor may be used in patients with severe neutropenia. Gut sterilization has been suggested, but its use is controversial. Patients should receive thromboprophylaxis and gastric ulcer prophylaxis. Sulfur donors (thiosulfate) have been used in animal studies, but there is no evidence that this is beneficial in humans.[2,17] Casualties with life-threatening injuries exemplified by large areas of erythema, painful eye lesions or lesions that hinder vision, or respiratory function should be transported to a facility that can provide tertiary care.[2] Patients who develop pulmonary symptoms within 4 to 6 hours of exposure have a very poor prognosis and may not benefit from transferring to a higher level of care.[2]

The psychological consequences of being exposed to HD are devastating. The exposure usually happens in the context of a military conflict, which in itself is a very stressful situation. Scarring and disfiguration are significant and carry severe psychological sequelae. Long-term complications can occur, and the concern for delay development of malignancies will always be present.[17] Prompt consultation with a behavioral health specialist, use of antidepressants, and early rehabilitation are crucial to ensure adequate recovery.

NERVE AGENTS

Nerve agents (exemplified by sarin, sabu, soman, and VX) were weaponized and stockpiled in the 1930s by the Germans but not used during the ensuing conflicts in which they participated. Only Iraq has used nerve agents against Iran in the 1984–1987 conflict. VX is one of the most toxic agents known to man; a single drop of VX can eliminate several hundred people. Although they are often described as gases, they are liquids at room temperature and spontaneously evaporate causing liquid and vapor hazards.[18] In simple terms, nerve agents act by inhibiting synaptic cholinesterase activity and inducing excessive cholinergic activity. Hence, patients exposed to nerve agents will have both muscarinic and nicotinic symptoms. Nerve agents are well absorbed through the alveolar-capillary membrane and distributed systemically throughout the blood inhibiting all cholinesterases.[18]

Nerve agent vapor is rapidly absorbed and produces clinical symptoms within minutes. Initially, nerve agents bind to papillary muscles and upper respiratory glands producing miosis, rhinorrhea, and salivation. Inhalation of the nerve vapor leads to bronchoconstriction and bronchorrhea. Circulating agent next affects the gastrointestinal tract causing cramping, abdominal pain, and defecation. The effect on the cardiovascular system varies depending on the intrinsic vagal tone, and the blood pressure and pulse response are unpredictable. Inhibition of peripheral acetylcholinesterase will result in twitching, fasciculations, and weakness. The muscle twitching is often confused with seizures. As the syndrome progresses, total flaccidity, arreflexia, and apnea may develop.[3] Excessive central cholinergic stimulation may result in coma, seizures, and central apnea.[18] Liquid nerve agent exposure through a wound requires careful monitoring as the patient may seem stable

initially but decompensate later on. Peripheral neuropathy, vestibulopathy, and neurobehavioral syndromes may complicate nerve agent exposure.[18,19]

The diagnosis of nerve agent poisoning is largely clinical. Confirmatory testing is done by measuring erythrocyte cholinesterase levels, but this test is not readily available in many centers. Furthermore, there is no correlation between the erythrocyte cholinesterase levels and the severity of the clinical syndrome. Lactic acidosis, leukocytosis, and elevated CK levels can also be present.[3] Sarin depresses medullary function and laboratory findings suggestive of hypoadrenalism may be present.[3]

Patients with nerve agent exposure often require ventilator support and intensivists need to be mindful that even patients with severe compromise may recover.[3] Ventilatory support may be needed because of bronchorrhea and bronchospasm, decreased level of consciousness, seizures, or generalized weakness. High airway resistance is a common critical care problem that responds to atropine administration.[2,3] The pharmacologic therapy of nerve agent poisoning relies on the administration of atropine, pralidoxime chloride, and diazepam.[2,18] Atropine is used in the field as an intramuscular injection via an autoinjector but is administered intravenous in the ICU. Atropine reverses cholinergic crisis at the muscarinic synapse. Since atropine does not bind to the nicotinic receptors, the neuromuscular signs are not treated with atropine. There is no true limit in the amount of atropine that can be given to an individual patient, and atropine therapy is titrated to the clinical response. Miosis is the last symptom to improve with treatment and may take up to 2 months to completely resolve. Treatment with atropine should be continued until respiratory effort improves and bronchial secretions are decreased. Pralidoxime chloride (2-PAM Cl) is used to reverse the neuromuscular (nicotinic) symptoms. Oximes reactivate catalytic cholinesterase and split nerve agents into harmless, easily removable compounds.[18] After a nerve agent binds to acetylcholinesterase, the resultant complex loses a side chain. This conformational change called "aging" has some clinical implications, as it renders the compound resistant to oxime activation. Aging rates for nerve agents vary significantly, but there is evidence that oximes work for certain agents even after 6 hours from exposure.[3] The military uses intramuscular diazepam for the treatment of seizures, but the civilian intensivist can use any intravenous benzodiazepine to control the seizures. Although initially seizures are generated by excessive cholinergic activity, later on other excitotoxic mediators also play a role.[19]

CONCLUSIONS

The critical care practitioner will likely be involved in the care of patients who are victims of chemical terrorism. A key understanding of the clinical presentation, laboratory findings, and prognostic elements is necessary in order to optimize outcomes and use resources in a rational manner. Aggressive supportive critical care is warranted in most situations as even severely compromised casualties can make significant recovery. Chemical terrorism incidents will likely overwhelm most health systems, and intensivists need to use the available resources judiciously recognizing which casualties are most likely to benefit from aggressive critical care. Although antidotes are available for some agents, meticulous critical care is the cornerstone of therapy for all chemical casualties. The psychological impact (on victims, clinicians, and community members) cannot be underestimated and requires intervention in order to prevent unnecessary hospital visits by the "worried well."

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